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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/373,230	08/12/1999	HARUKI OKMURA	OKAMURA=2E	2359

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EXAMINER
JIANG, DONG

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 10/04/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/373,230	OKMURA ET AL.	
	Examiner	Art Unit	
	Dong Jiang	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 July 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3-9,11,14 and 16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-9,11,14 and 16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED OFFICE ACTION

Applicant's amendment filed on 19 July 2006 is acknowledged and entered. Following the amendment, claims 3-5, 7, 8, 11, 14 and 16 are amended.

Currently, claims 3-9, 11, 14 and 16 are pending and under consideration.

Withdrawal of Objections and Rejections:

The rejection of claims 3-6, 14 and 16 under 35 U.S.C. 112, second paragraph, as being indefinite is withdrawn in view of applicant's amendment and argument.

New Matter Rejection:

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3-6, 11, 14 and 16 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the reasons of record set forth in the last Office Action mailed on 24 January 2006, at pages 3-4.

Applicants argument filed on 19 July 2006 has been fully considered, but is not deemed persuasive for reasons below.

At pages 11-12 of the response, the applicant argues that the specification discloses an amino acid sequence of SEQ ID NO:2 in which one or more amino acids are replaced, added or deleted, indicating that these sequences have less than 100% homology to SEQ ID NO:2, which are easily obtainable, that mouse IL-18 has 91.9% homology to rat IL-18 while the homologies with bovine IL-18 remain less than 70%, and the recitation of "at least 90% homologous" does not include bovine IL-18, and that the present invention is a pioneer invention and is believed to deserve wider protection. This argument is not persuasive because, once again, the issue is not whether making a variant of a molecule is routine, or whether there are other IL-18 sharing more or

less than 90% homology to SEQ ID NO:2, rather, the issue is that the recited limitation "at least 90% homologous to" represents a specific scope, which is not described in the specification as originally filed, and cannot be predicted or anticipated from the general disclosure of "variants" having one or more amino acids are replaced, added or deleted.

With respect to "pioneer invention", there is no law or rule indicating that a pioneer discovery would be entitled to lower patent standard or requirement. MPEP indicates that under 37 CFR 1.121, (f), no amendment may introduce new matter into the disclosure of an application, and that if the new matter has been entered into the claims or affects the scope of the claims, the claims affected should be rejected under 35 U.S.C.112, first paragraph, because the new matter is not described in the application as originally filed (MPEP 608.04).

Rejections under 35 U.S.C. 112:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 11 remains rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for the reasons of record set forth in the last Office Action mailed on 24 January 2006, at page 4, and for the reasons below.

The newly amended part (6) of the claim recites "binds to a monoclonal antibody specific to an ... protein having ... SEQ ID NO:2 *or having an amino acid sequence which is at least 90% homologous to ... SEQ ID NO:2*", which still reads on a sequence variant of SEQ ID NO:2. A monoclonal antibody to such a variant may or may not be SEQ ID NO:2 specific, and therefore, it does not help to define the structure of the claimed protein.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3-6, 11, 14 and 16 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for claims limited in scope to the IGIF of SEQ ID NO:2, and a specific variant of said protein, which has an amino acid sequence of SEQ ID:2 where residue 70 is methionine or threonine, does not reasonably provide enablement for with claims to a variant having physicochemical and functional properties listed in parts (1) to (4) of claim 3, and having the amino acid sequence at least 90% homologous to SEQ ID:2 (claims 3 and 16, for example), reacting with a mAb specific to a variant at least 90% homologous to SEQ ID:2 (claim 11, for example), or a hybridization variant having the amino acid sequence at least 90% homologous to SEQ ID:2 (claim 14, for example), while substantially having the biological activity of (3). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims, for the reasons set forth in the previous Office Actions.

Although several species of IL-18 have been isolated by now. However, at the time the invention was filed, only mouse IL-18 of SEQ ID NO:2 was known, and the specification does not disclose any correlation between the sequence structure and functional activity of the protein. Further, the specification does not provide any guidance or working example as to how to make the encompassed variants. Therefore, undue experimentation would be required of the skilled artisan to make the claimed invention in its full scope.

Claims 3-6, 11, 14 and 16 remain further rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the reasons of record set forth in the previous Office Actions.

Rejections Over Prior Art:

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 3-9, 11, 14 and 16 remain rejected under 35 U.S.C. 102(b) as being anticipated by Nakamura *et al.* (*Infect. Immun.* 61: 64-70, 1993), for the reasons set forth in the previous Office Actions, paper Nos. 4, 7 and 13, and the Office Actions mailed on 9/9/04, 6/3/05, and 1/24/06.

Applicants argument filed on 19 July 2006 has been fully considered, but is not deemed persuasive for reasons below.

At pages 15-19 of the response, the applicant mainly repeats the same arguments as previous ones, such as the differences between the prior art "factor" and the presently claimed protein in source of isolation, MW, activity when treated with SDS-PAGE, purity, specific activity after purification. These arguments have been repeatedly addressed in detail in the previous Office Actions, and they are not persuasive for the reasons of record. Further, as indicated in the previous Office Actions (mailed on 7/3/01 and 3/21/03, for example), the post filing date publication by Okamura (from the same group) et al. (*Infection and Immunity*, 1995, 63(10):3966-72) discloses a purified murine IGIF from the liver with the same physiochemical and biological properties as the claimed IGIF, and further indicates that the same molecule was also demonstrated in the serum factor that was previously reported (by Nakamura) to have an apparent molecular mass of 75 kDa by gel filtration (and 50-55 kDa on SDS-PAGE). Moreover, Okamura demonstrates that the molecular mass of 75 kDa IGIF was reduced to 19 kDa on 0.1% SDS-PAGE in the presence of DTT, and the N-terminal amino acid sequence is the same as that of IGIF from the liver. Okamura concludes "thus IGIF in the serum sample was proved to be the same IGIF as that found in the liver exact" (page 3969, the second paragraph of the left column). Therefore, it is *evidenced* by the Okamura reference that the two factors isolated by Nakamura and Okamura, respectively, are the same protein regardless their seemingly difference in "physical appearance". Thus, as Okamura's factor is the same as that of the present invention, Nakamura's factor would render the presently claimed protein not novel anticipate.

With respect to applicants new argument on page 15 of the response (the last item in the Table) that Nakamura's factor is incapable of inducing IFN-γ production in IFN-γ producing cells with the factor alone, but is capable of doing so in the presence of IL-2, ConA … (page 67), whereas the polypeptide of the present invention is capable of inducing IFN-γ production in IFN-

whereas the polypeptide of the present invention is capable of inducing IFN-γ production in IFN-γ producing cells with the polypeptide alone, it is not persuasive because the result from the comparable experiment (to Nakamura's experiment) disclosed in the instant specification (pages 25-26, Experiment 2-4(a)) shows that the protein induced about 2-2,000 IU IFN-γ and about 2-200 IU IFN-γ when the T-cells were respectively incubated with and without 0.02-10 pg/ml of ConA. The result is clear: in the absence of ConA, the amount of IFN-γ production (2-200 IU) induced by the present protein is less significant, and comparable to that (16 ±5 IU, Table 3) induced by Nakamura's factor.

With respect to applicants argument on page 18 of the response that Dr. Haruki Okamura is one of the authors of both Nakamura and Okamura references, and Dr. Okamura shows in the declaration filed on 12/1/05 that even as one of the authors of the Nakamura reference, he did not consider the "factor" to be the polypeptide of 19±5 kD in MW. This argument is not persuasive because it is irrelevant as to how or what Dr. Okamura considered at the time, and the evidentiary fact has proven that the two factors are the same.

Conclusion:

No claim is allowed.

Advisory Information:

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication should be directed to Dong Jiang whose telephone number is 571-272-0872. The examiner can normally be reached on Monday - Friday from 9:30 AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Dong Jiang, Ph.D.
Patent Examiner
AU1646
9/20/06

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